Instruction 1(b)

FORM 4

Check this box if no longer subject to Section 16. Form 4 or Form 5 obligations may continue. See

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Filed pursuant to Section 16(a) of the Securities Exchange Act of 1934

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or Section 30(h) of the Investment Company Act of 1940 2. Issuer Name and Ticker or Trading Symbol 5. Relationship of Reporting Person(s) to Issuer 1. Name and Address of Reporting Person* (Check all applicable) IONIS PHARMACEUTICALS INC [IONS **HOUGEN ELIZABETH L** Director 10% Owner Officer (give title Other (specify below) below) (Last) (First) (Middle) 3. Date of Earliest Transaction (Month/Day/Year) **SVP Finance & CFO** C/O IONIS PHARMACEUTICALS, INC. 07/01/2018 2855 GAZELLE COURT 4. If Amendment, Date of Original Filed (Month/Day/Year) 6. Individual or Joint/Group Filing (Check Applicable Line) (Street) X Form filed by One Reporting Person 92010 **CARLSBAD** CA Form filed by More than One Reporting (City) (State) (Zip) Table I - Non-Derivative Securities Acquired, Disposed of, or Beneficially Owned 4. Securities Acquired (A) or Disposed Of (D) (Instr. 3, 4 and 5) 1. Title of Security (Instr. 3) 2. Transaction 2A. Deemed 5. Amount of 6. Ownership 7. Nature **Execution Date** Transaction Securities Form: Direct of Indirect if any (Month/Day/Year) (Month/Day/Year) Code (Instr. Beneficially (D) or Indirect Beneficial Owned Following (I) (Instr. 4) Ownership 8) Reported (Instr. 4) (A) or (D) saction(s) Price Code ν Amount (Instr. 3 and 4) 07/01/2018 **J**(1) Common Stock 07/01/2018 274(1) \$35.4195 14,774 D Α Table II - Derivative Securities Acquired, Disposed of, or Beneficially Owned (e.g., puts, calls, warrants, options, convertible securities) 1. Title of 3A. Deemed 3. Transaction 6. Date Exercisable and 7. Title and 8. Price of 9. Number of 10. 11. Nature 5. Number Derivative Conversion Execution Date Transaction Expiration Date (Month/Day/Year) Ownership of Indirect (Month/Day/Year) Derivative Security (Instr. 3) Securities Securities or Exercise if anv Code (Instr. Security Form: Beneficial Price of Derivative (Month/Day/Year) 8) Securities Underlying Derivative (Instr. 5) Beneficially Direct (D) Ownership Acquired Owned or Indirect (I) (Instr. 4) (Instr. 4) (A) or Disposed Security Security (Instr. 3 Following and 4) Reported of (D) Transaction(s) (Instr. 3, 4 (Instr. 4) and 5) Amount Number Expiration Code (A) (D) Exercisable Title Shares

Explanation of Responses:

1. Reporting 274 shares acquired under the Ionis Pharmaceuticals, Inc. Amended and Restated 2000 Employee Stock Purchase Plan on July 1, 2018. These 274 shares may not be sold until January 2, 2019.

Remarks:

/s/Patrick R. O'Neil, attorneyin-fact 07/03/2018

** Signature of Reporting Person Date

Reminder: Report on a separate line for each class of securities beneficially owned directly or indirectly.

- * If the form is filed by more than one reporting person, see Instruction 4 (b)(v).
- ** Intentional misstatements or omissions of facts constitute Federal Criminal Violations See 18 U.S.C. 1001 and 15 U.S.C. 78ff(a).

Note: File three copies of this Form, one of which must be manually signed. If space is insufficient, see Instruction 6 for procedure.

Persons who respond to the collection of information contained in this form are not required to respond unless the form displays a currently valid OMB Number.